MEDICAL PROCEEDINGS

MEDIESE BYDRAES

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REDAKSIONEEL · EDITORIAL

PULMONALE ALVEOLÊRE PROTEÏNOSE

Elders in hierdie uitgawe publiseer ons 'n verslag deur prof. B. J. P. Becker, van die Universiteit van die Witwatersrand, Johannesburg, oor die eerste geval van pulmonale alveolêre proteïnose wat in Suid-Afrika teëgekom is. Die eerste beskrywing van hierdie besondere toestand het so kort gelede soos 1958 in die V.S.A. verskyn, maar, soos professor Becker daarop wys, is gevalle sedertdien in Kanada, Engeland, Italië en Nieu-Seeland waargeneem. Die herkenning van die siekte in Suid-Afrika bewys dat dit 'n wydverspreide kwaal is, ondanks die feit dat dit pas onlangs ontdek is.

Die kliniese beeld is van progressiewe longversaking (sonder enige spesifieke kenmerke) wat weerstand teen behandeling bied. Dit ontsluit dus die deur vir 'n baie breë differensiële diagnose. Inderdaad, die meeste gevalle presenteer aanvanklik gewoonlik as atipiese pneumonie, waarvoor daar radiologiese bevestiging is.

Dit is onwaarskynlik dat die siekte in die verlede oor die hoof gesien is. Die wit konsolidasie in die longe wek makroskopiese agterdog, en die mikroskopiese voorkoms is besonder kenmerkend en spesifiek. Dit moet derhalwe beskou word as 'n nuwe siekte wat gedurende die afgelope paar jaar ontstaan het.

Daar is veel te sê vir die sienswyse dat die longletsel waarskynlik 'n nie-akute virusinfeksie is, geassosieer met 'n outo-immune liggaamsreaksie op die longweefsel. As 'n virus by die saak betrokke is, moet dit 'n nuwe virus of 'n onlangse mutasievorm wees. Die geldigheid van die virushipotese kan alleen getoets word deur die demonstrasie van 'n stygende

PULMONARY ALVEOLAR PROTEINOSIS

Elsewhere in this issue Prof. B. J. P. Becker, of the University of the Witwatersrand, Johannesburg, publishes an account of the first case of pulmonary alveolar proteinosis to be recorded in South Africa. The condition was first described in the U.S.A. as recently as 1958 and, as Professor Becker points out, cases have now been observed, in addition, in Canada, England, Italy and New Zealand. The recognition of the disease in South Africa indicates its widespread nature despite its recent discovery.

The clinical picture is one of progressive lung failure without any particularly specific features, and resistant to treatment. It thus opens the door to a very wide differential diagnosis. Indeed, these cases usually present initially as an atypical pneumonia, of which there is radiological confirmation.

It is unlikely that the disease has been overlooked in the past. The white consolidation in the lungs raises macroscopic suspicions and the microscopic appearances are highly characteristic and specific. It must therefore be regarded as a new disease which has developed within the last few years.

There is much to be said for the view that the lung lesion probably represents a non-acute virus infection associated with an auto-immune body response to the lung tissue. If a virus is involved, it must be a new virus or a recent mutant. The validity of the virus hypothesis can only be tested by demonstrating a rising titre of specific antibodies and the immunological process should be detectable by the demonstration of lung auto-antibodies. Neither

titer van spesifieke teenstowwe, en die immunologiese proses behoort bespeurbaar te wees deur die demonstrasie van long-outo-teenstowwe. Geeneen van hierdie twee laboratoriumprosedures is tot dusver op dié probleem toegepas nie.

Die ergste deel van die letsel skyn aan die alveolêre voeringselle en die elastiese weefsel van die alveolêre wand te wees. Dit verduidelik die hoogs kenmerkende mikroskopiese voorkoms, en beperk die outo-immune liggaamsreaksie tot die longe. Dit is interessant om bespiegelinge te doen oor die moontlikheid dat subkliniese infeksies die pulmonale elastiese weefsel kan vernietig is dus, deur 'n outo-immune liggaamsmeganisme, 'n grondslag vir die verduideliking van die verspreide blasie-agtige emfiseem kan verskaf.

Professor Becker vestig die aandag ook op die feit dat die naam wat aan die nuwe siekte gegee is, waarskynlik nie volkome geskik is nie. Met die oog op die histochemiese studies kan dit miskien beter beskryf word as 'n muko-lipoïdose wat met 2 opvallende morfologiese veranderings geassosieer is:

1. Elastolise,
2. Alveolêre selvermenigvuldiging en degenerasie.

Aan hierdie 2 prosesse moet die lipied- en mukusryke alveolêre inhoud toegeskryf word.

Hoewel 'n ernstige prognose waarskynlik net op 'n klein aantal gevalle van toepassing is, is dit noodsaaklik dat kliniste op hul hoede en in staat moet wees om die toestand te herken. Slegs op hierdie manier is dit moontlik om geskikte virus- en ander laboratoriumstudies te onderneem. Hierdie volledige ondersoek gedurende die leeftyd van die pasiënt kan waardevolle gegewens i.v.m. die etiologie van die toestand beskikbaar stel, en kan aanleiding gee tot 'n suksesvoller behandelingsmetode as wat tot dusver moontlik was.

JOHNSON & JOHNSON SE TOEKENNINGS VIR NA-GRAADSE KLINIESE STUDIE IN SUID-AFRIKA

VIER BEURSE TOT BESKIKKING VAN ALGEMENE PRAKTISYNS IN 1961

Hierdie toekennings is moontlik gemaak deur 'n toelae wat deur Johnson & Johnson (Pty.) Ltd., Posbus 727, Oos-Londen, beskikbaar gestel is.

Die keurkomitee ('n volkome onafhanklike raad van mediese praktisyns) bestaan uit die volgende:

Prof. S. F. Oosthuizen (Pretoria) *Voorsitter*;
Dr. P. F. H. Wagner (Oos-Londen), *Ondervoorsitter*;
Dr. H. A. Shapiro (Johannesburg) *Eresekretaris*;
Dr. Beck de Villiers (Bloemfontein);
Dr. H. Grant-Whyte (Durban);
Prof. H. W. Snyman (Pretoria).

Aansoeke word ingewag van geregistreerde *algemene praktisyns* wat ten minste 7 jaar lank aktief in Suid-Afrika praktiseer.

Die beurse is bedoel vir na-graadse kliniese studie, en nie vir mediese navorsing nie. Hulle

of these two laboratory procedures has yet been applied to this problem.

The brunt of the lesion appears to be on the alveolar lining cells and the elastic tissue of the alveolar wall. This explains the highly characteristic microscopic appearances and limits the auto-immune body reaction to the lungs. It is interesting to speculate on the possibility that subclinical infections may destroy pulmonary elastic tissue and thus, by an auto-immune body mechanism, provide a basis for explaining generalized vesicular emphysema.

Professor Becker also draws attention to the fact that the name with which the new disease has been christened is probably not entirely apt. In view of the histochemical studies, it would be better described as a muco-lipoidosis, which is associated with 2 striking morphological changes:

1. Elastolysis.
2. Alveolar cell proliferation and degeneration.

These 2 processes account for the lipid and mucus rich alveolar contents.

Although a grave prognosis applies probably only to a small percentage of the cases involved, it is important to alert clinicians to the need for recognizing the condition. It is only in this way that the appropriate virus and other laboratory studies can be made. This fuller investigation during the lifetime of the patient may provide valuable data to establish the etiology of the condition and so lead to a more successful method of treatment than has been possible hitherto.

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Applications are invited from registered *general practitioners* who have been in active practice in South Africa for at least 7 years.

The Bursary is intended for post-graduate clinical study and not for medical research. It is available for not less than a 2-month period

is beskikbaar vir 'n tydperk van nie minder as 2 maande nie aan enige Mediese Skool in Suid-Afrika.

Die totale waarde van iedere beurs is R600.

Die kandidaat moet 'n kort uiteensetting van sy voorgestelde studiekursus verstrek, en moet aandui na watter Mediese Skool hy voornemens is om te gaan.

Geen betalings sal aan 'n suksesvolle applikant gedoen word tot tyd en wyl hy die keurkomitee tevrede gestel het dat hy vir 'n tydperk van na-graadse studie aan 'n Suid-Afrikaanse Mediese Skool aangeneem is nie.

Aansoek moet gedoen word op die voorgeskrewe vorm wat verkrygbaar is van:

Dr. H. A. Shapiro (*Eresekretaris*),
Keurkomitee,
Johnson & Johnson se Toekennings vir
Na-graadse Kliniese Studie,
Posbus 1010, Johannesburg.

Vier beurse is beskikbaar vir toekenning gedurende 1961.

Sluitingsdatum vir aansoeke: 1 Augustus 1961.

RESIPROSITEIT BUITE DIE STATEBOND

Noudat Suid-Afrika hom aan die Statebond onttrek het, word in sommige kringe gevrees dat die huidige resiprositeitsreëlings tussen Suid-Afrika en sekere Statebondslande tot 'n einde kan kom.

Die veronderstelling waarop hierdie vrees berus, is volkome vals. Resiprositeit is in die eerste en vernaamste plaas afhanklik van die onderlinge aanvaarding van professionele opleidings-, eksamen- en bevoegdheidstandaarde. Dit het niks met die politiek te make nie, en in beginsel is daar dus geen rede vir vrees, uithoofde hiervan, vir enige onderbreking van ons resiprositeitsreëlings binne die Statebond nie, ten spyte van ons politieke status as 'n onafhanklike en outonome republiek buite die Statebond.

Dit is verblydend om te verneem dat die Suid-Afrikaanse Geneeskundige en Tandheelkundige Raad inderdaad reeds tot 'n ooreenkoms met die Algemene Geneeskundige Raad en die Algemene Tandheelkundige Raad in the Verenigde Koninkryk geraak het oor voortgesette resiprositeit tussen Groot-Brittanje en die Republiek Suid-Afrika. Enige struikelblok in die weg van die instandhouding van hierdie onderling voordelige reëling sou nie van politieke oorsprong gewees het nie. Dit kon egter ontstaan het uit die ongelyke en eensydige behoeftes in verband met domisilie wat in ons eie Wet neergelê word. Gelukkig het die aanbeveling van ons Geneeskundige Raad dat hierdie eensydige vereiste opgehef moet word, die werklike belemmering vir voortdurende resiprositeit tussen Suid-Afrika en die Verenigde Koninkryk uit die weg geruim.

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The total value of each Bursary is R600.

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Johnson & Johnson Awards for Post-Graduate Clinical Study,
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Four Fellowships will be available for Award during 1961.

Closing date for Applications: 1 August 1961.

RECIPROCITY OUTSIDE THE COMMONWEALTH

Misgivings have been expressed in some quarters that, with South Africa's withdrawal from the Commonwealth, the existing reciprocity arrangements between South Africa and certain Commonwealth States may be terminated.

The premise on which such fears may have been founded is totally fallacious. Reciprocity depends primarily on the mutual acceptance of standards of professional training, examination and competence. It is not politically determined and, in principle, there is therefore no reason (on this account) to fear any interruption of our reciprocity arrangements within the Commonwealth, despite our political status as an independent and autonomous republic without membership of that Commonwealth.

It is gratifying to learn that, in fact, our South African Medical and Dental Council has completed negotiations with the General Medical Council and the General Dental Council in the United Kingdom for continued reciprocity between Great Britain and the Republic of South Africa. The stumbling block to a persistence of this mutually beneficial arrangement would not have been political. It might, however, well have arisen from the unequal and unilateral requirements regarding domicile required by our own Act. Fortunately, the recommendation by our Medical Council that this one-sided requirement be abandoned, has removed the real obstacle to continued reciprocity between South Africa and the United Kingdom.

PULMONARY ALVEOLAR PROTEINOSIS

A REPORT OF A CASE AND A HISTOCHEMICAL INVESTIGATION OF THE CONDITION

B. J. P. BECKER, M.D.

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Rosen, Castleman and Liebow[1] described 27 cases of an apparently unique pathological entity which they called 'pulmonary alveolar proteinosis.' Since then further cases have been reported.[2-7] Cases have now been observed in the U.S.A., Canada, England, Italy and New Zealand.

This report describes a typical case observed in the Union of South Africa.

CASE REPORT

Mr. C. B., a 39-year-old White male, was admitted to the Johannesburg General Hospital on 14 May 1957. His main complaint was severe breathlessness, and double vision for 3 weeks.

Past History. The patient, who had been a hotel manager since his discharge from the Army in 1945, stated that he had never had any illnesses of note till one year before admission, when he had a febrile illness with pleuritic type pains over the upper part of the chest posteriorly and a slight non-productive cough. There was no haemoptysis, no breathlessness and no cyanosis. He was treated in hospital on antibiotics for 25 days. All his symptoms disappeared, but he was told that the radiological abnormality had not cleared. Nevertheless he was discharged from hospital and continued his work as an hotelier. At first he felt quite well but gradually a 'heavy feeling' developed in his chest; then over a period of 7 months he developed such exertional dyspnoea that he could no longer mount stairs. A recurrence of pleural pain caused him to consult a physician, who pointed out that he was cyanosed and that clubbing of the fingers was present. Lung biopsy was performed at this stage. This was not diagnostic but a Hammon-Rich syndrome was suggested and steroid therapy was commenced (Meticorten 5 mg., *t.d.s.*). Five months of this therapy brought no relief. In the last 3 weeks before admission his breathlessness had become so severe that he could barely manage to walk and even shaving brought on shortness of breath. Concomitant with the rapid increase in exercise intolerance, he noticed double vision in all directions, somewhat better when one eye (either one) was closed.

The patient had not at any time been exposed to underground mining, to industrial, war or other irritating gas. He had smoked about 40 cigarettes daily for some years.

Physical Examination. Examination on admission showed an adult male patient in obvious severe dyspnoea, deeply cyanosed (generalized) and somewhat euphoric. There was clubbing of fingers and toes and a persistent, dry, non-productive cough. The pulse rate was 120 per minute, regular and of good volume. The respiration rate was 40 per minute and the temperature 98°F.

Cardio-Vascular System. The jugular venous pressure was not raised. There was no sign of peripheral oedema, no hepato-splenomegaly and no ascites. The maximum cardiac impulse was in the 5th interspace within the midclavicular line. There was no right ventricular heave and the heart was not enlarged to percussion. On auscultation P2 was accentuated and split with the pulmonary element louder than the aortic element and not remarkably affected by respiration. There were no murmurs.

Lungs. The chest movement was good but air entry was poor, vocal fremitus and vocal resonance were equal and normal on both sides. There were no rhonchi but bilateral diffuse sticky crepitations were heard showering at the end of inspiration especially.

Nervous System. There was no strabismus or paralysis of the extra-ocular or intra-ocular muscles. Examination of the fundi showed bilateral disc oedema with distended tortuous veins, numerous small linear radiating paraarterial haemorrhages and numerous darker diffuse multiform paravenous haemorrhages. Both retinae were plethoric. The rest of the nervous system showed no significant abnormality.

X-Ray. X-ray at this time showed woolly opacities, particularly at the base and hilar regions (Fig. 1).

TREATMENT AND PROGRESS

On increasing steroid hormone therapy and on bed rest the patient gradually improved so that the oxygen requirements became a few minutes per hour by day, and sleeping with the oxygen mask with low O_2 flow during the night. Cyanosis, however, was persistent except when on oxygen, and lung signs did not change.

After 14 days of therapy thick yellowish sputum was being produced. A short course of antibiotics was commenced and the purulence disappeared, only to reappear 3 weeks later associated with an intermittent temperature, pain in the left chest posteriorly, but with no change in signs.

However, at this time the patient developed severe soreness of the mouth with scattered white patches over the tongue, cheeks and posterior pharynx which were resistant to local and general treatment. The patient's condition gradually deteriorated, large amounts of purulent sputum were being produced and cyanosis was persistent, even in the oxygen tent.

Death occurred 2 months after admission.

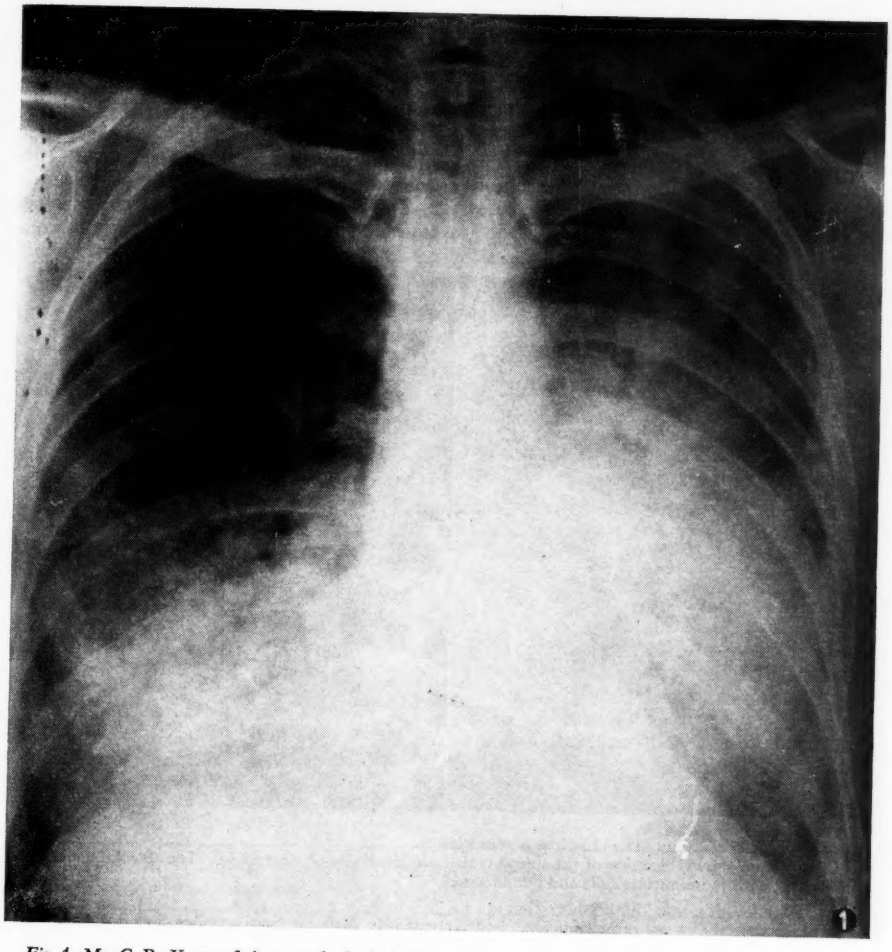

Fig. 1. Mr. C. B. X-ray of chest on final admission.
The plate shows feathery and cotton-wool densities with a tendency to concentrate around the hilar regions.

AUTOPSY

Autopsy was performed on 18 July 1957, 48 hours after death. The subject was a rather undernourished male of 39 years, 5′ 8″ in height. There was well-marked clubbing of the fingers and intense cyanosis. There was no oedema and no jaundice.

Nothing abnormal was discovered in the skin, subcutaneous tissues, muscles, joints, mucous membranes, breasts or superficial lymph glands.

Serous Sacs. The peritoneal and pericardial sacs were normal.

Pleurae. Evidence of bilateral chronic fibrous pleurisy was present, especially at the bases, with a superadded acute fibrinous exudate.

Lungs. Both lungs were exceptionally heavy (Left = 1,820 g.; Right = 2,080 g.). Large emphysematous bullae were present at the apices. The visceral pleura was covered with a fibrinous exudate. The lungs were completely consolidated and white in appearance. Here and there small ragged cavities had formed. The bronchi were full of purulent material. *Monilia albicans* was cultured from lung scrapings.

Spleen. Weight, 140 g. It was soft and pink.

Kidneys. The kidneys showed the presence of multiple ragged abscess cavities. Culture from these showed the presence of *M. albicans.*

The remaining body organs showed no significant pathological changes.

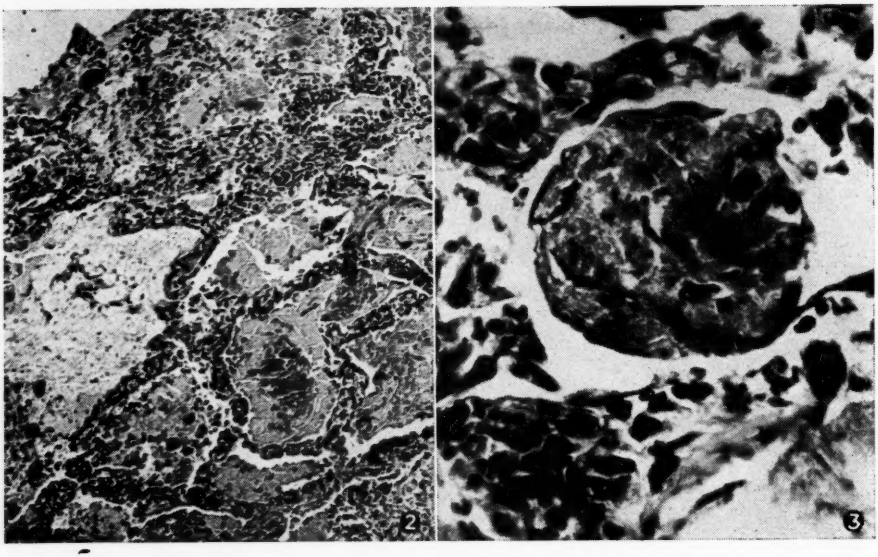

Fig. 2. Section of Lung: (H and E, low power view).
The section shows dilatation of the alveoli with granular, eosinophilic material. The alveolar walls are infiltrated with mononuclear cells and lymphocytes.

Fig. 3. Section of Lung: (high power view).
The section shows an early laminated body, apparently forming from swollen and degenerating alveolar septal cells.

Cardio-Vascular System. The heart weighed 390 g. The left ventricular segment weighed 110 g. (normal); the right ventricular segment 79 g. (upper limit of normal = 74 g.). All valves were competent and healthy. The coronary arteries showed slight atheroma. The muscle was pale and showed minute abscesses. Cultures from these showed the presence of *M. albicans.*

HISTOLOGY

Lungs. The characteristic feature consisted of a granular, eosinophil material which filled and often dilated large groups of alveoli and small bronchioles (Fig. 2). In this granular material intact alveolar phagocytes were occasionally observed and, on polarization, acicular crystals, sometimes few, sometimes many, were evident.

In some alveoli, in addition to the granular material clumps of basophilic, hyperchromatic alveolar septal cells were present. Often these showed foamy or eosinophilic degeneration of their cytoplasm. The lesion was not diffuse, large involved areas were sited next to less involved or even comparatively normal ones. Inflammatory cell infiltration was not striking but here and there there were aggregates of plasma cells and in a few areas a scattering of neutrophil leucocytes. Hyaline thrombi were present in the small blood vessels. The lesion was typical of the lesion described by Rosen *et al.*[1] as a pulmonary alveolar proteinosis. The laminated bodies described by them were also frequently seen (Fig. 3). In addition, the lungs showed severe infection with *Monilia albicans* (confirmed by culture).

The histology of the remaining body organs was characterized by pyaemic abscesses in which *Monilia albicans* was abundant. Apart from this no significant pathological features were observed.

SUMMARY OF CASE

(*a*) A young male hotelier suffers an attack of 'atypical pneumonia' which necessitated hospitalization for 25 days.

Radiological mottling of the lungs had not cleared on discharge from hospital.

(*b*) Thereafter he suffered from a relentlessly progressive pulmonary failure, barely held in check by bed rest, O_2 therapy and increasing steroid hormones.

(*c*) He died a year after his initial attack with a terminal generalized *Monilia albicans* infection and lung failure.

(*d*) Autopsy and subsequent histological examination showed the typical features of *pulmonary alveolar proteinosis.*

INVESTIGATIONS

1. THE NATURE OF THE GRANULAR MATERIAL IN THE ALVEOLI

TABLE 1: METHODS FOR LIPIDS

Method	*Result*	*Significance*	*Reference*
Auto-fluorescence	Silvery-white to yellow clumps	—	—
Phosphine 3R (F/S 0·1% Aq. 3 minutes)	Silvery-white clumps	Lipids	Popper[8]
Magdala Red (F/S 0·1% Aq. 3 minutes)	Yellow clumps	Lipids	Haitinger[9]
Thioflavin S (F/S 0·01% 10 minutes)	Blue clumps	Lipids	Haitinger[9]
Oil Red O(F/S)	Finely granular neutral fats in phagocytes lying free, and in degenerating septal cells	Neutral fats	Lillie[10]
Sudan Black B (F/S & P/S)	Black granular and clumped material	Lipids	McManus[11]
Phospho-Molybdic Acid Method (F/S)	Blue clumped material (free)	Choline—containing lipids	Landing *et al.*[12]
Acid Haematin	Blue-black clumps: reduced after pyridine extraction	Phospholipids (or nucleoproteins)	Baker[13]
Copper Phthalocyanin (F/S and P/S)	Blue clumps	Phospholipids	Kluver and Barrera[14]
Okamoto's Mercury Diphenylcarbazone	Bluish-violet clumps. Remains positive but reduced after 48 hours ether extraction	Phospholipid Sphingomyelin probable	Ueda[15] Ueda[15]

(*Continued overleaf*)

Method	*Result*	*Significance*	*Reference*
Performic-Acid Schiff (F.S.)	Red clumps	Phospholipid or cerebroside	Lillie[16]
Modified Molisch	Negative	No sugar containing lipids	Diezel[17]
Modified Brückner	Negative		
Fischler's Method (F/S)	Negative	No fatty acids	Pearse[18]
Okamoto's Method (Cholesterol)	Blue green clumps	Cholesterol and/or Esters	Ueda[15]
Feigin's Method	Positive (green) in control only	Cholesterol Esters	Feigin[19]
Phenyl-hydrazine Formazan (Without periodic acid oxidation)	Red-brown clumps	Auto-oxidising lipids	Karnovsky and Dean[20]
Nile blue	Red and blue clumps (also + with sudan black)	Neutral and acidic lipids	Cain[21]

SUMMARY

The methods for lipids show the presence of intracellular and extracellular neutral fat and phospholipid; clumped extracellular neutral fat, phospholipid and cholesterol esters. The phospholipids present include both lecithin and sphingomyelin.

TABLE 2: METHODS FOR CARBOHYDRATES

Method	*Result*	*Significance*	*Reference*
Periodic acid Schiff	++(Diastase fast)	Mucoprotein Glycoprotein Glycolipid	Pearse[18]
Toluidine Blue	Red metachromasia in Aq. mount. Not alcohol fast: becomes alcohol after sulphation	Acid mucopolysaccharides	Pearse[18]
Alcian Blue (pH 2)	+	Acid mucopolysaccharide or connective tissue mucins	Pearse[18]
Hale	+	Acid mucopolysaccharides or connective tissue mucins	Pearse[18]
Toluidine Blue after Hyaluronidase (testicular extraction)	+	Acid mucopolysaccharide, connective tissue mucins (CSA type B)	Pearse[18]
Feyter Enclosure Method	++Rose—Red	Lipids and various mucins	Pearse[18]

SUMMARY

Sulphation (sulphuric acid and acetic anhydride) increased the red metachromasia tremendously and also rendered it alcohol fast. Acetylation (40% acetic anhydride in anhydrous pyridine for 24 hours at 25°C.) reduced but did not abolish the PAS reaction,

and this was restored by de-acetylation (0.1 N KOH for 45 minutes at room temperature).

The methods for carbohydrates show the presence of abundant mucins of mixed type—epithelial and connective tissue together with mucoproteins and glycoproteins.

METHODS FOR PROTEINS

The Millon reaction,[22] the Mercury-Bromphenol Method,[23] the Morel-Sisley Method (Lillie)[31] and the Ninhydrin-Schiff Method[24] all gave *faint positive results*, indicating the presence of traces of protein. The post-coupled benzylidene reaction for indoles[25] showed occasional positive clumped aggregates, as did the Sagaguchi reaction for arginine.[22] The alkaline tetrazolium method (Pearse[18]) showed both blue and red aggregates, i.e. lipid and non-lipid reducing groups. The presence of reducing groups was confirmed by a positive ferric-ferrocyanide method.[26] The Thioglycollate-Ferric Ferricyanide Method for disulphides[27] was negative.

The methods for proteins showed the presence of proteinaceous material in very limited amount compared to the abundant lipid and carbohydrate. The clumped material giving a positive reaction for tryptophan was thought to be possibly fibrin and this was tentatively confirmed by similar clumps staining blue with Mallory's PTAH method.

2. THE CRYSTALS

Frozen sections under polarized light showed abundant acicular crystals, free and clumped, and abundant minute anisotropic granules. All these had largely disappeared in paraffin sections.

In frozen sections the crystals failed to dissolve in weak acid (3% H_2SO_4) in weak alkali (3% NaOH) or in 95% alcohol, ether, acetone or pyridine (30 minutes to 18 hours each at room temperature). They dissolved however in pyridine at 60°C. for 1 hour. The crystals did *not* fluoresce. In frozen sections stained with Sudan Black B, most of the material in the alveoli stained black. In transmitted light the crystals also appeared black, but when polarized (after Sudan Black B staining) some were blue, some were red and some were unstained. Lennert and Weitzel[28] claim that lipids capable of eliciting metachromasia are dipoles (Zwitterions). Pearse[18] believes that further examination of the mechanism is necessary. According to Höber[29] Zwitterions include aminoacids, peptides and aminoacids at their iso-electric points, and cites Cohen to include urea and phospholipids. Attempts to colourise the crystals with methods for proteins (Millon; Mercury Bromphenol Blue) proved negative. Available evidence suggests that the crystalline material is of lipid origin.

3. GENERAL METHODS

(*a*) *Elastica.* The Verhoeff method showed surprisingly little intact elastic tissue in the alveolar walls. This was confirmed by fluorescence (auto-fluorescence and alkaline primulin). Auto-fluorescence of a section of a case of pulmonary alveolar proteinosis from the Armed Forces Institute of Pathology (AFIP 851936) confirmed the loss of elastic tissue. The Verhoeff stain and fluorescence methods showed positive staining material in the alveolar contents, which could represent elastic tissue residues.

Severe elastolysis is a prominent and important feature and could account for some of the mucinous content and some of the lipid (sphingomyelin) content of the alveolar material.

(*b*) *Micro-organisms.* Apart from the presence in some areas of *M. albicans*, search for micro-organisms was negative. In particular no cysts of *Pneumocystis carinii* were observed (Gomori Methamine Silver Method).

Inclusion bodies were sought in sections stained by the Haematoxylin-Shorr method, with negative results.

SUMMARY OF INVESTIGATIONS

The alveolar contents show the presence of abundant lipids of all types (neutral fats, phospholipid, protein-bound lipid, cholesterol ester) in amorphous and crystalline form. This confirms the finding of Rosen *et al.*[1] of an astonishingly high fat content (4–5 times normal) in chemically analysed lungs of alveolar proteinosis.

The abundant lipids lie in a pool of mixed mucins (mucopolysaccharides, mucoproteins, glycoproteins) of both epithelial and connective tissue type; and in this pool are traces of proteinaceous material. A more appropriate name for the condition would be 'pulmonary mucolipoidosis'.

The muco-lipoidosis is associated with 2 striking morphological alterations:

1. Elastolysis.
2. Alveolar cell proliferation and degeneration.

These 2 processes account for the lipid and mucus rich alveolar contents.

DISCUSSION

In this case, and in many of the cases described by Rosen *et al.*,[1] the onset of the condition was marked by an attack of 'atypical' pneumonia.

Thereafter followed a phase of progressive dyspnoea and cyanosis, culminating in lung failure. In several cases of Rosen *et al.*'s series,[1] terminal superimposed fungal infection occurred. In other cases, progress was less rapid and some even showed clinical and radiological improvement and survived at least 5 years after the initial diagnosis by lung biopsy. Clearly, the course varies from case to case.

Nothing definite is known regarding the etiology. The condition shows some similarities to *Pneumocystis carinii* infections but search for this parasite has proved negative in all reported cases. The onset with atypical pneumonia, the marked epithelial proliferation and subsequent degeneration suggest a viral infection, and the lung changes bear a certain resemblance to those found in fatal cases of psittacosis, as described by Wilson,[30] in which a pneumonia with confluent lobular distribution occurs and the alveoli are filled with a granular exudate of indeterminate character, the walls of the alveoli being thinned and inconspicuous. Cells in the alveoli exudate consist of swollen and degenerated cells from the alveolar lining and neutrophil leucocytes are present in only small numbers. Severe epithelial damage occurs in the bronchioles. Hyaline thrombi were found in the capillaries. Future cases should be investigated with this possibility of a chronic virus infection of this type in mind.

The alveolar contents (muco-lipoidosis with traces of protein) are derived in all probability from the residues of cell degeneration and the elastolysis.

No treatment has as yet proved of much avail. Corticoids and antibiotics do not materially affect the course.

SUMMARY

(*a*) A case of pulmonary alveolar proteinosis occurring in Johannesburg, South Africa, has been described.

(*b*) The case followed the typical pattern of a febrile illness followed by progressive lung insufficiency, and death occurred as a result of lung failure and terminal *Monilia albicans* infection.

(*c*) Histological and histochemical investigation revealed a picture of progressive alveolar cell proliferation and degeneration together with severe elastolysis and an accumulation of abundant mixed mucoid and lipid substances with traces of protein in the dilated alveoli.

(d) The possibility is raised that the disease represents a persistent subacute or chronic viral respiratory infection.

REFERENCES

1. Rosen, S. H., Castleman B. and Liebow, A. A. (1958): New Eng. J. Med., **258**, 1123.
2. Friedman, B. and Strickland, C. E. (1958): J. Tenn. State Med. Assoc., **51**, 507.
3. Moertel, C. G., Woolner, L. B. and Bernatz, P. E. (1959): Proc. Staff Meetings Mayo Clin., **34**, 152.
4. Levinson, B., Jones, R. S., Wintrobe, M. M. and Cartwright, G. E. (1958): Blood, **13**, 959.
5. Payseur, C. R., Konwaler, B. E. and Hyde, L. (1958): Amer. Rev. Tuberc., **78**, 906.
6. McDowell, C., Williams, S. E. and Hinds, J. R. (1959): Australasian Ann. Med., **8**, 137.
7. Jones, C. C. (1960): Amer. J. Med., **29**, 713.
8. Popper, H. (1944): Physiol. Rev., **24**, 205.
9. Haitinger, M. (1938): *Fluoreszenmekroskopie*, Akad. Verlag, Leipzig.
10. Lillie, R. D. (1944): Stain Tech., **19**, 55.
11. McManus, J. F. A. (1946): J. Path. Bact., **58**, 93.
12. Landing, B. H., Uzman, L. L. and Whipple, L. A. (1952): Lab. Invest., **1**, 456.
13. Baker, J. R. (1946): Quart. J. Micro. Sci., **85**, 1.
14. Klüver, H. and Barrera, E. (1953): J. Neuropath. Exp. Neurol., **12**, 400.
15. Ueda, M. (1952): Hyoyo J. Med. Sci., **1**, 117.
16. Lillie, R. D. (1952): Stain Tech., **27**, 37.
17. Diezel, P. B. (1954): Virchows Arch., **326**, 89.
18. Pearse, A. G. E. (1960): *Histochemistry*. London: J. & A. Churchill, Ltd.
19. Feigin, I. (1956): J. Biophys. Biochem. Cytol., **2**, 213.
20. Karnovsky, M. L. and Dean, H. W. (1955): J. Histochem. Cytochem., **3**, 85.
21. Cain, A. J. (1947): Quart. J. Micr. Sci., **88**, 383.
22. Baker, J. R. (1947): Quart. J. Micr. Sci, **88**, 115.
23. Bonhag, P. F. (1955): J. Morphol., **96**, 381.
24. Yasuma, A. and Ichikawa, T. (1953): J. Lab. Clin. Med., **41**, 296.
25. Glenner, G. G. and Lillie, R. D. (1957): J. Histochem. Cytochem., **5**, 279.
26. Chévremont, M. and Fréderic, L. (1943): Arch. Biol., **54**, 589.
27. Adams, C. W. M. (1956): J. Histochem. Cytochem., **4**, 23.
28. Lennert, K. and Weitzel, G. (1952): Zeit. Wiss. Miko., **61**, 20.
29. Höber, R. (1956): *Physical Chemistry of Cells and Tissues*. Philadelphia: Blakiston Co.
30. Wilson, G. H. (1930): J. Path. Bact., **33**, 957.
31. Lillie, R. D. (1957): J. Histochem. Cytochem., **5**, 528.

THE ROUTINE USE OF INTRAMUSCULAR SYNTOCINON

IN THE LATE SECOND STAGE OF LABOUR

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Post-partum haemorrhage and post-partum morbidity can be significantly reduced by administering oxytocics at the end of the second stage of labour.[1] The intravenous administration of ergometrine preparations (Ergometrine or Methergin) has been advocated by many authors. However, this is quite impracticable in a large African maternity hospital where nurses and midwives are not allowed to give intravenous injections. We have tried to overcome this difficulty by using the combination of Ergometrine with Hyaluronidase (Ergo-Rondase) or by giving intramuscular injections of synthetic oxytocin (Syntocinon, Sandoz) with the birth of the anterior shoulder.

Syntocinon is synthetic oxytocin, an octapeptide first synthesized by du Vignaud[2] and produced at the Sandoz Laboratories by a method discovered there by Boissonas in 1955.[3]

Konzet[4] showed that Syntocinon had physiological and chemical properties identical with those of naturally occurring oxytocin, with the added advantage that Syntocinon is completely free from vasopressin and other foreign polypeptides.

Numerous reports[5-9] have demonstrated the usefulness of Syntocinon for the induction of labour, during labour for hypotonic contractions,[10] after delivery to reduce blood loss,[11] and during the puerperium to relieve breast engorgement.[12, 13]

Our purpose was to investigate the value of administering Syntocinon routinely in the late second stage of labour intramuscularly and to assess its influence on average blood loss, amount of post-partum haemorrhage, retained placenta, breast engorgement and breast abscesses, involution of the uterus and puerperal morbidity.

MATERIAL AND METHODS

Syntocinon is available in ampoules containing 10 Units in 1 ml. (5 Units in 0.5 ml.) and in ampoules containing 1 Unit in 1 ml. (Ampoules of 2 ml. containing 2 Units). We have used the ampoules of 2 ml. containing 2 Units throughout.

All normal deliveries at the African Maternity Hospital during the years 1958 to 1960 formed the basis of this series.

The first 500 cases were given 2 Units of Syntocinon intramuscularly after birth of the infant and before delivery of the placenta and the membranes. The next 2,400 cases were given 2 Units of Syntocinon intramuscularly with the delivery of the anterior shoulder of the foetus.

One hundred and fifty cases were given Ergo-Rondase (Evans)* intramuscularly with the birth of the anterior shoulder.

All abnormal cases were excluded from this investigation.

DEFINITIONS

Retained Placenta. A placenta which was retained for 30 minutes was regarded as a retained placenta and manual removal was carried out.

Blood Loss. Direct measurement of blood loss, although difficult and subject to a margin of error, was the method used to determine the amount of blood lost.

Breast Engorgement. A case of breast engorgement was classified as such if the breasts were tense and the patient complained of severe pain.

RESULTS

(*a*) *Blood Loss and Post-Partum Haemorrhage.* Table 1 summarizes the results achieved with:

i. 2 Units Syntocinon intramuscularly after birth of the infant.

ii. 2 Units Syntocinon intramuscularly with the anterior shoulder.

iii. Ergo-Rondase intramuscularly with the anterior shoulder.

iv. Controls.

The routine use of the oxytocic drugs given with the birth of the anterior shoulder of the foetus diminishes blood loss during the third stage of labour. Syntocinon appears to be more effective than ergometrine in controlling the uterine bleeding. There is a distinct advantage in giving the Syntocinon with the birth of the anterior shoulder. If, however, this is not done, then it should be given immediately after the birth of the infant.

The routine use of the oxytocic drugs lessens the time taken for the placenta to be expelled. The tone of the uterus is improved with these drugs, but it would appear that Ergometrine has a more selective action on the cervix than has Syntocinon. This is reflected by the fact that in all the cases of retained placenta occurring after Ergometrine had been used,

* Ergometrine Maleate B.P. 0.5 mg. and Hyaluronidase 330 International Units.

the cervical os was clamped down, preventing the expulsion of the placenta. This is also reflected by the increased incidence of retained placenta occurring in the Ergometrine series as compared with the control series. Although MacDonald[14] recommended in 1958 that oxytocin should not be used to expedite delivery of the placenta, as it would appear to cause more frequent banding of the uterus, our findings do not support this statement. On the contrary, the incidence of retained placenta after 2 Units of Syntocinon given with the anterior shoulder, was 40 times less than in the control series.

TABLE 1

	Syntocinon 2 Units (Intramuscular Injection After Birth of Infant)		*Syntocinon 2 Units (With Birth of Anterior Shoulder)*		*Ergo-Rondase (Intramuscular Injection with Birth of Anterior Shoulder)*		*Controls*	
Cases:	500		2,400		150		1,000	
	Primiparae	*Multiparae*	*Primiparae*	*Multiparae*	*Primiparae*	*Multiparae*	*Primiparae*	*Multiparae*
Third Stage (Average Duration in Minutes)	8·1	7·7	7·7	6·93	7·7	7·6	9·0	8·1
Blood Loss (Average in Oz.)	5·7	6·9	4·9	5·4	5·46	6·82	7·6	7·95
Number of Cases where Blood Loss Exceeded 20 Oz.	2·7%		1·9%		3%		5·6%	
Retained Placenta:	0·2%		0·05%		3%		2%	

(*b*) *Breast Engorgement.* Numerous reports have shown the value of Syntocinon in disorders of lactation. In the majority of these trials Syntocinon was used for breast engorgement after the engorgement had appeared. The present series (Table 2) shows that breast engorgement is less frequent in those cases where Syntocinon had been used routinely in the third stage of labour.

TABLE 2

	Syntocinon	*Ergo-Rondase*	*Controls*
Number of Cases	2000	150	1000
Breast Engorgement	1 (0.05%)	3 (2%)	21 (2.1%)
Breast Abscess	0	1	15

(*c*) *Involution of the Uterus and Post-Partum Morbidity.* Syntocinon has been shown to increase the involution of the uterus. Table 3 indicates that Syntocinon does promote involution of the uterus and reduces post-partum morbidity:

TABLE 3

	Syntocinon	*Ergo-Rondase*	*Controls*
Average Height of Uterus 2nd day Post-Partum	5.9 inches	6 inches	6 inches
3rd day Post-Partum	5 inches	5.5 inches	5.5 inches
4th day Post-Partum	3 inches	4.1 inches	4.1 inches
Morbidity Rate: 100.4° F and over	3.65%	7.58%	7.55%

(*d*) *Side Effects.* We found Syntocinon free from side effects, and agree with Stewart and Nelson[12] in this respect. In no case was nausea and vomiting directly attributable to the use of Syntocinon, and in only 1.8% of cases did a transient rise of blood pressure occur. The rise never exceeded 20 mm. Hg. With Ergo-Rondase nausea and vomiting occurred in 7% of cases and a rise of blood pressure in 3.3%. Most surprisingly, Syntocinon did not only not increase the rate of retained placenta but actually reduced it to 0.05%, compared with 2% in the controls.

SUMMARY AND CONCLUSIONS

The routine intramuscular administration of Syntocinon for the active management of the third stage of labour was investigated in African parturients.

Syntocinon shortens the third stage, reduces blood loss and reduces the incidence of retained placenta. It also reduces the incidence of breast engorgement, hastens involution and reduces the incidence of post-partum morbidity.

The results are best if an intramuscular injection of 2 International Units of Syntocinon is given with the birth of the anterior shoulder.

No serious side effects were encountered.

I wish to express my appreciation to Sandoz Limited for supplies of Syntocinon and to Evans Medical for the Ergo-Rondase.

REFERENCES

1. de Villiers, J. N. and du Toit, J. P. (1960): S. Afr. Med. J., **34**, 561.
2. du Vigneaud, V., Ressler, C., Swan, J. M., Roberts, C. W. and Katsoyannis, G. P. (1954): J. Amer. Chem. Soc., **76**, 3115.
3. Boissonnas, R. A., Guttman, S. A., Jaquenoud, P. A., and Walier, J. P. (1955): Helv. Chim. Acta, **38**, 1491.
   Boissonnas, R. A. *et al* (1956): Nature, **178**, 260.
4. Konzett, H., Berde, B. and Cerletti, A. (1956): Schweiz. Med. Wschr., **86**, 226.
5. Bainbridge, M. N., Nixon, W. C. W., Schild, H. O. and Smyth, C. N. (1956): Brit. Med. J. **1**, 1133.
6. Francis, H. H. and Francis, W. J. A. (1956): Brit. Med., J., **1**, 1136.
7. Bösch, K. and Käser, O. (1956): Schweiz. Med. Wschr., **86**, 229.
8. Mayes, B. T. and Shearman, R. P. (1956): J. Obstet. Gynaecol. Brit. Emp., **63**, 812.
9. Nixon, W. C. W. and Smyth, C. N. (1957): J. Obstet. Gynaecol. Brit. Emp., **64**, 35.
10. Nixon, W. C. W. and Smyth, C. N. (1958): Triangle, **3**, 239.
11. Stewart, R. H. and Slezak, R. M. (1958): Obstet. Gynecol., N.Y., **11**, 295.
12. Stewart, R. H. and Nelson, R. N. (1959): Obstet. Gynecol. N.Y., **13**, 204.
13. Whitelaw, M. J., Carsen, A. J. and Sanfilippo, P. (1959): Med. Times, **87**, 681.
14. MacDonald, A. D. (1958): Practitioner, **180**, 71.

LEDERMYCIN OINTMENT

A CLINICAL TRIAL

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The number of antibiotics available is now so great and their efficiency is so high, that any newcomer to this field must possess unique properties if it is to win an established position as a therapeutic agent. In 1957 a tetracycline compound with such claims was discovered. Known as demethylchlortetracycline (DMCT), it was isolated by McCormick and his co-workers[1] from a mutant of the strain *Streptomyces aureofaciens Duggar*. It was quickly shown that its particular virtue lay in its ability to produce higher and more sustained levels of antibacterial activity in the blood of humans than those obtained with tetracycline, chlortetracycline and oxytetracycline; in its stability; and in its greater activity against the common laboratory assay organisms, *Bacillus cereus* #, Streptococcus 98 and Staphyloccus 209P.[2, 3] Because of its stability in the body and its slow rate of renal clearance it produces *in vivo* antibacterial activity of the order of 3 times that of tetracycline and is consequently effective in much lower doses and for longer periods than that drug, when given systemically. Like other tetracyclines, it is also active on the surface of the skin. The requirements of a first-class local application are that:

1. It should be efficient.
2. It should have a low sensitizing potential.
3. Its cost should be reasonable.
4. It should be easy to apply and easy to remove; and
5. It should not stain unduly.

A short clinical trial with an ointment containing 0.5% DMCT has shown that it possesses these attributes in no small measure. Twenty successive patients, with a varied assortment of the primary infectious processes and secondary pyodermas of the skin commonly seen in routine dermatological practice, were treated (Table 1). In all cases, any infection present cleared promptly. There was no effect,

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however, on any underlying pathological abnormality which did not of itself have an infective cause.

Two patients complained of irritation while using the preparation. The first, a highly strung youth of 17 was given the ointment for excoriated acne with secondary serocrusting. Two days later itching developed. There was no visible evidence of local reaction and patch-testing was negative. There was likewise nothing to suggest that increased photosensitivity (as has been reported with oral DMCT)[4] was responsible and the symptoms quickly subsided when the ointment was discontinued. The second patient to complain of discomfort was a 56-year-old woman with an infected hypostatic leg ulcer. She had previously take oral DMCT without any reaction, but within 3 days of starting the ointment she developed burning and itching. Examination revealed some erythema and commencing vesiculation around the treated area and a patch-test with the ointment applied to her forearm was positive at 48 hours. A further patch-test with DMCT suspension, in a concentrate of 60 mg. in 1 c.c., was negative and the inference is that her sensitivity was to the ointment base and not the antibiotic itself.

Neither the nature of the infecting organisms in the cases treated, nor their *in vitro* sensitivity, was investigated. The cost of these tests is such that they cannot reasonably be performed routinely on all cases reporting for examination; but the main laboratory operating in the area reports that an analysis of all 63 swabs from infected skin lesions submitted to it within the 12-month period January–December 1960 showed that some grew more than 1 organism; but that the overall distribution frequency was *Streptococcus haemolyticus* 10; *Staphylococcus aureus* 51; *B. pyocyaneus* 5; Achromobacter 2; *S. faecalis* 5; *E. coli* 8; *S. viridans* 4; *B. proteus* 2. While this result gives an approximate picture of the predominant organisms in the area, it is open to certain criticism. It reflects the position only so far as the more resistant infections go. Because of the economic factors already mentioned, it is usual in this country to swab only those problem cases in which there is no response to the antibiotic prescribed when the patient is first seen. Cases which respond promptly are not swabbed.

It was considered impracticable to carry out a controlled trial using only the ointment base for alternate patients; or by the method of

TABLE 1: RESULTS

Case No.	*Age*	*Sex*	*Diagnosis*	*Result*	*Length of Treatment (in Days)*
1	49	M	Impetigo	Well	5
2	9	M	Impetigo—scalp	Well	5
3	10	F	Impetigo—scalp	Well	6
4	9 months	F	Eczema, infantile—impetigenized	Infection controlled	5
5	15	M	Impetigo—scalp	Well	6
6	16	M	Acne excorieé	Local irritation. Patch-tests negative	2
7	48	M	Infected biopsy wound	Well	10
8	13 months	M	Papular urticaria—infected	Infection controlled	7
9	28	F	Impetigo	Well	7
10	2	F	Impetigo	Well	7
11	35	M	Impetigo	Well	7
12	25	M	Atopic eczema—impetigenized	Infection controlled	5
13	75	M	Impetigo	Well	9
14	3	M	Impetigo	Well	9
15	9	M	Scabies—impetigenized	Infection controlled	7
16	5	F	Eczema—impetigenized	Infection controlled	7
17	21	M	Sycosis barbae	Well	7
18	56	F	Hypostatic ulcer	Ulcer healed. Local irritation. Patch-test positive	20
19	10	M	Infectious eczematoid dermatitis	Well	7
20	12	F	Impetigo	Well	10

simultaneous paired comparison using the opposite limbs as a control. The colour of DMCT is such that it was not possible to simulate it accurately without the addition to the ointment base of dyes which have of themselves been known to cause reactions of an allergic nature and it was considered that to use a visibly different control would have been valueless.

SUMMARY

The results of this small series of cases show that 0.5% DMCT ointment is an effective local application for the control of secondary infection in skin lesions.

2 of the patients treated complained of irritation. Neither gave a positive patch-test to DMCT in solution but 1 was positive to DMCT ointment. The inference is that this patient's sensitivity was to the ointment base and not to the antibiotic itself.

In several patients a double pathology was present, the rash consisting of an underlying disorder complicated by secondary coccal infection. In these cases the DMCT ointment controlled the infection but had no effect on the rash.

OPSOMMING

'n Klein reeks van gevalle toon dat 0.5% DMCT salf, 'n doeltreffende plaaslike behandeling is vir die beheer van sekondêre infeksie van vel letsels.

Twee pasiënte het gekla van irritasie met gebruik van die middel. Huidtoetse is uitgevoer by hierdie pasiënte, en DMCT oplossing het geen reaksie veroorsaak nie. DMCT salf het egter by een 'n positiewe resultaat gelewer, en dit blyk asof die sensitiwiteit hier te wyte is aan die salf-basis en nie die antibiotikum as sulks nie.

By sommige pasiënte was dubbele patologie teenwoordig—die onderliggende primêre toestand met sekondêre infeksie daarby. By hierdie gevalle het DMCT 'n goeie uitwerking gehad op die infeksie. Die primêre toestand het egter nie gereageer op die antibiotiese behandeling nie.

I am indebted to Dr. I. Bersohn and to Dr. L. Schrire of the South African Institute for Medical Research for supplying me with the swab reports analysed in the article and for permitting me to use this information.

The Ledermycin ointment used in the trial was provided by the Lederle Laboratories Division of the American Cyanamid Company.

REFERENCES

1. McCormick, J. R. D., Sjolander, N. O., Hirsch, U., Jensen, E. R. and Doerschuk, A. P. (1957): J. Amer. Chem. Soc., **79**, 4561.
2. Kunin, C. M. and Findland, M. (1958): New Eng. J. Med., **259**, 999.
3. Sweeney, W. M., Hardy, S. M., Dornbush, A. C. and Reugsegger, J. M. (1959): Antibiotic Med., **9**, 13.
4. Fuhrman, P. L. and Drowns, B. V. (1960): Arch. Dermatol., **82**, 244.

SOME ASPECTS OF MEDICAL PHOTOGRAPHY

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On a recent visit to several European countries I was able to study some of the applications of photography to medicine.

The developments both in black-and-white and particularly in colour photography have been most impressive. Lithography (the use of printers' machinery) in various hospitals and medical schools, was a completely new aspect.

Ilfords Limited (*London*). Here the use of subdued lighting in photographing post-mortem specimens and medical instruments was shown to be most effective. The underlying principle is that instead of the 45° conventional lighting, one flood lamp is used as a reflector from the wall and another flood lamp is placed at an angle less than 45°. The angle selected is judged by the photographer. This method eliminates gross highlights from wet specimens and stainless steel instruments.

A new method of storing and filing of 3¼ inch slides was also demonstrated. Series of rails to which transparent pockets are attached for holding the slides, are erected on either side of an X-ray viewing screen. By rolling out the pockets in front of the viewer, selections may be made rapidly by reference to the index on the cupboard doors. At the Christie Holt Cancer Hospital this system is used for filing and storing 35 mm. transparencies. This method appeared to be most effective.

The London School of Medical Photography. This may not be known to many in South Africa. It provides a course in medical photography. Technicians preparing for the final examinations of the Institute of British Photo-

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graphers spend one year full-time attending lectures and doing practical work in the photographic departments of the London Medical Schools. The fee for this course is 50 guineas.

Guy's Hospital. It was interesting to observe that the overhead gantry of lights has been superseded by a more effective and convenient method of lighting, that of electronic flash. The plastic white background in the studio is likewise now replaced by paper of the desired colour. This paper comes in rolls 6-8 feet wide and of any desired length. When soiled, the paper is discarded by tearing off the roll and a new section put into place.

The *Medical Art Section* attached to Guy's Hospital offers training in medical art and illustration, provided the applicant has had 1-2 years' drawing experience. Only one student is accommodated per year, as there are few openings in this field.

Walter Bird's Studio. Bird certainly deserves the reputation that 'he paints with his lights'. In his handling of portraits, the placing of his lights revealed the reason for his outstanding success in this field. Briefly, one flood light is positioned directly on to the face and a 'fill in' on the opposite side; then, with selected background, one or two lights are directed on to this background. The use of either one or two spotlights for back lighting is optional. In his studio there was a demonstration of colour photography using a 3,000 Joule electronic flash unit. The results with such a high light value were outstanding as compared with low output units.

Birmingham. It was of interest to note a plaque at the entrance of the photographic unit inscribed:

'This Unit was established with a grant of £1,500 by the British Institute of Cinematography.'

The studio of this department was most impressive, being about 60 feet long and 20 feet wide. Besides giving ample room for patient photography, it also accommodates apparatus used in the copying of charts and graphs, X-ray and photostats.

Manchester Royal Infirmary Photographic Department. This is by far the most advanced in the United Kingdom; it represents a model worth copying. It supplies a photographic service to the Royal Infirmary, the Medical School, the Dental School, the Eye Hospital, the G. & O. Hospital, the Christie Holt Cancer Hospital and the Salford Hospital.

The staff at Headquarters comprises, a full-time Director, a Chief Technician, a Medical Illustrator, a Senior Technician, 3 Juniors and one full-time Secretary.

Christie Holt Cancer Hospital: One Senior Technician and 2 juniors.

Salford Hospital: One Junior Technician.

The accommodation at Headquarters consists of: Director's office, secretarial office, reception room, filing room, store room, drawing office, printers' room, finishing room, 4 dark rooms, studio with dressing cubicle, copying room, and a room for the lithographic machine.

The staff is appointed only from applicants who have had previous satisfactory experience or who hold certificates of the Institute of British Photography.

The senior members do all the camera work in the studio or in the hospitals. The juniors handle developing and printing of negatives, loading of film, mixing of solutions and do all the finishing work. The secretary attends to the administration of reception, typing, cataloguing, distribution of finished photographs or slides and prepares charts for photography using the Vari-Typer. The Director and Chief Technician supervise the work at all stages but, in addition, the Chief Technician is responsible for making and repairing equipment, and participates in the research of the Unit.

In this department the graphic arts are fully used. An illustrator is of considerable value in assisting authors with the preparation of diagrams, graphs or illustrations. A very simple method has been evolved whereby the author pencils on the selected size of graph paper, the main lines and contours of the illustration. This is next traced off by the illustrator on to a second sheet of graph paper. The drawing is then completed accurately. The correct words and figures are set up on a hand printing press and added to the drawing in the appropriate places. The illustrator makes considerable use of Zip-a-tone paper in preparing diagrams.

The Vari-Typer is very valuable in producing clear Tables for photography. This machine is equipped with special characters and figures designed for photography. A very useful adjunct is that complicated Tables with many columns of figures or words may be condensed in size and yet be legible for photography.

A small lithograph machine is also used. These 2 methods have led to much saving of time and money in preparing graphs, slides and the printing of small articles.

In the photographic section the use of litho contrast film was demonstrated. This has replaced the conventional line film for reproducing black-and-white drawings. Litho contrast film provides a conventional negative for black-and-white slides or prints. The film may also be reversed by a bleaching process to make

a positive negative, which on enlargement will give a white reproduction and a black background. This may, of course, be coloured by photo tints. The cine section had shown considerable progress. A first-grade cine camera with all accessories, costing about £1,000, was in use. This camera is only sold to professional users and the condition of sale requires that it be regularly maintained by the suppliers. An interesting and valuable film produced by this department was *Fire Hazards in a Hospital.* It was used in the training programme of the nursing staff.

The Manchester Department will be willing to accept selected technicians from South Africa for short concentrated practical courses in medical photography.

Newcastle-upon-Tyne. Here the University Photographic Department is one of the largest in the United Kingdom. It supplies a service to the University, the Medical School and the teaching Hospitals. The workshop facilities are impressive. Equipment of all kinds, particularly cine, was designed and made according to the needs of the projects. A sound-proof previewing theatre, seating 20, was part of this department. The lithographic section, the largest in the U.K. Universities, with the Vari-Typers, again demonstrated how necessary these methods are for producing first-class work. A special technique of cine recording of high speed revolutions of ships' screws, using strobe (continuous electronic flash lighting) in a wind tunnel was demonstrated. This is the only unit of its kind in any United Kingdom University. A cine camera with built-in strobe lighting is mounted in the tunnel. The screw is yellow-brown in colour with no flaws visible to the naked eye. When the maximum revolutions are obtained, the lighting is switched on, and the screw takes on an aluminium colour, with the flaws in the shape of black zigzagging lines, visible to the naked eye; these lines are recorded by the cine camera.

Groningen, Holland. The photographic department here is a large one, serving the University, the Medical School and the hospitals. Seventeen technicians are employed and their new building, soon to be completed, will be 3 stories high.

Of special interest was one of the copying enlargers. It has a 3-turreted set of lenses with the appropriate condensers. By a simple manipulation any size negative from 35 mm. to 7 inch by 5 inch can be enlarged or reduced.

The plastic acid fixing bath incorporated a small motor, allowing all prints to circulate, thus ensuring complete and uniform fixing.

The dark room benches were made of plastic material, chemically resistant and easily cleaned.

Professor Decking, Head of the Ophthalmological Department has great interest in photography as applied to ophthalmology. This has led to his filming his operations on the eye without any assistance. A cine camera is mounted on a movable cross piece, which incorporates the lights. The camera is enclosed in a sterile compartment and positioned over the eye and, by means of a foot switch, any part of the operation can be recorded by the surgeon. He has also modified a fundus camera to incorporate flash lighting. The transparencies produced were of a very high standard and were extremely valuable in medical instruction. He has constructed an ophthalmic stereoscopic camera of his own design, together with a unique projector. The transparencies are mounted on a treadmill type of apparatus in a container. A handle works the treadmill and viewing is done through a special lens designed by Professor Decking.

Belgium: *The Gevaert Colour School.* This School offered a 10-day course in colour photography, which I attended. This course comprises the theoretical aspects of colour, followed by practical work in the processing of Gevacolor and colour printing of the negatives. Other courses available are photomicrography, lithography and black-and-white photography. The facilities are modern and impressive. The courses may be taken in English and are held throughout the year.

As far as University, Medical School and Hospital services are concerned, the trend is toward centralization. Large departments fully equipped, except for special needs, cover University work in all fields. Clinical and Medical School photography is a major section in such large departments.

Centralization avoids the expense of much duplicate equipment and accommodation. Workshop facilities likewise become more economic and much can be done on the premises in the maintenance and development of new equipment. Training of personnel becomes more thorough and the quality of work improves as a result.

The personnel of these central units usually comprised a Professor of a Department as Director, a Chief Photographer or Technician, a full-time secretary, one or two Senior Assistant Technicians and 2 or 3 juniors. Three units in the United Kingdom employ medical practitioners on a full-time basis, as Directors of the Photographic Departments.

It was clear that the full-time secretaries were extremely valuable in ensuring the smooth and efficient administration of large departments.

The progress of medical photography has indicated that careers may be enjoyed in this branch. Although much perhaps remains to be done to improve conditions of service, there is little doubt that in Universities and the Medical Schools, there is opportunity for young men and women to take up very satisfying work in this speciality.

As is to be expected, colour work is receiving more attention both in the still and cine fields. The availability of more powerful electronic flash equipment enables this development to proceed rapidly. Colour slides and coloured prints are being requested more and more frequently by authors and lecturers.

The increasing use of medical illustrators, improved typewriting methods and the lithograph machines in the preparation of graphs, drawings, slides, etc. was evident.

The need for improving South African facilities, standards and techniques is considerable. There is little doubt in the light of the growth of medical research and its dissemination by publication or by lecture, that the medical photographer is an important member of the team.

It is of interest that the importance of medical photography in a Medical School and a teaching hospital, has reached such a stage that the First International Congress on Medical Photography was held in Germany in September 1960.

It was stimulating to note that many of the medical staff participated in the Congress. Lectures were delivered in the main by Professors and medical practitioners.

This tour was made possible for me by the courtesy and financial aid from Protea Holdings Travelling Grant, University of the Witwatersrand, A. D. Bensusan Bursary Fund.

I wish to thank Prof. G. A. Elliott, Prof. J. H. Gear and Dr. A. D. Bensusan for their help and guidance.

NOTES AND NEWS : BERIGTE

Dr. Ellis Cooper, M.B., Ch.B., D.Obst., R.C.O.G., M.R.C.O.G., has commenced practice as an Obstetrician and Gynaecologist at 1105 Ingrams Building, Corner of Twist and Kotze Streets, Hillbrow, Johannesburg. (*Telephones*:— *Rooms*: 44-9235; *Residence*: 41-3513).

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Dr. Percy S. Terespolsky has joined Dr. A. V. Bird and Dr. S. Jacobson in partnership at 118 Lister Buildings, Jeppe Street, Johannesburg, and at 107 Tafelberg, Esselen Street (opposite the Princess Nursing Home), Hillbrow, Johannesburg. (*Telephones*:— 22-7275 and 44-4444).

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UNIVERSITY OF CAPE TOWN

REFRESHER COURSE FOR GENERAL PRACTITIONERS

24-28 JULY 1961

A Refresher Course for General Practitioners will be held, consisting of lectures, ward rounds and demonstrations in Medicine, Surgery, Obstetrics and Gynaecology and the Specialties at appointed times between 8 a.m. and 5.30 p.m. daily from 24 to 28 July 1961. Practitioners who wish to spend a further 3 days to attend special clinics, departments, operations, etc. are welcome to do so but, unfortunately, will not be able to remain in Medical Residence for this extended period as the students will have returned.

The Course will probably include the following:

(*a*) Wards Rounds with senior members of the teaching staff in Medicine, Surgery, Dermatology, Paediatrics, Obstetrics and Gynaecology.

(*b*) Panel discussions by groups of consultants on a variety of subjects including the following:

Everyday surgical procedures. Common surgical lesions in infants and children. Acute cardiac disease. Hormones in practice. Acute trauma—Head, Abdominal and Thoracic. Common obstetrical and gynaecological problems. Asthma and other allergic disorders.

A feature of these discussions is that ample opportunity will be provided for members of the panel to answer questions raised by the Practitioners attending the Course.

(*c*) Demonstrations by the Consultant Staff of the following:

Anaesthetic Techniques and Minor Surgery. Minor Gynaecological Procedures. Everyday Orthopaedic Methods. Minor Medical and Paediatric Procedures.

(*d*) A lecture-demonstration on the following subjects:

Respiratory Infections of Childhood. Common Skin Diseases.

(*e*) Sessions: 'Any Questions.'

Special sessions will be provided in Ophthalmology and Otorhinolaryngology, Paediatrics (in which a panel of members will answer questions asked by General Practitioners on any subject not covered by the programme of the Course).

The number of Practitioners that can be accepted for the Course is restricted.

The fee for the Course will be R10.50, payable in advance to the Registrar, University of Cape Town. This fee should not be sent until the applicant has been notified that he will be admitted to the Course.

Board and lodging will be available at Medical Residence for those desiring it (and for their wives) at a charge of R 2.10 per day per person.

Applications for admission to the Course, stating whether residential accommodation will be required

or not, should be submitted as soon as possible to:

The Registrar, University of Cape Town, Private Bag, Rondebosch.

They should reach him before Monday, 5 June 1961.

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IRON DEFICIENCY RESEARCH UNIT

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

A research Unit which will study on a world-wide basis the problem of iron deficiency anaemia in human beings has been established in the Department of Medicine of the University of the Witwatersrand by the World Health Organization.

The head of the Unit will be Dr. T. H. Bothwell (Physician (Tutorial) in the Department). Iron deficiency anaemia is regarded as a major public health problem and one of the greatest causes of ill health and death in under-developed areas throughout the world.

The Unit has been established as a result of a recent visit to Johannesburg by Prof. C. A. Finch, a leading American authority on iron metabolism, who visited a number of countries at the invitation of the World Health Organization to investigate the problem of iron deficiency anaemia.

As a result of his recommendations, a pilot research programme has been approved whereby 4 laboratory units are being established—one each in the United States, in Venezuela, in India (New Delhi) and in Johannesburg. The Units will work in close collaboration to define the incidence and causation of the disease and then the study will be expanded to include other areas.

Although iron deficiency anaemia is not a serious problem in South Africa, because of the high iron content of the Bantu diet, its incidence in Central Africa is very high and it was considered that Johannesburg was the most suitable centre on the African Continent for the analysis of certain tissue specimens which will be sent here from the other 3 units. Once the causative factors of the disease in different areas have been determined, an extended research programme will be embarked upon.

Dr. Bothwell has recently returned from America where he acted as Associate Professor at the University of Washington Medical School, Seattle, for 2 months. He also visited Thailand as a guest of the International Atomic Energy Agency, a division of the World Health Organization, at a symposium where he read a paper on *The Application of Radio-Active Isotopes in the Study of Iron Metabolism.*

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THE NUTRITION SOCIETY

ADVANCE NOTICE OF 143RD MEETING

The following is the programme of a symposium to be held in Oxford on Saturday, 15 July 1961 on *Nutrition and Metabolic Defects.* (*Chairman*: Sir Hans Krebs, F.R.S.).

Dr. H. M. Sinclair (Oxford): *Historical Aspects of Inborn Errors of Metabolism.*

Dr. Philip Evans (London): *Clinical Account of Some Metabolic Defects.*

Dr. L. I. Woolf (Oxford): *Nutrition in Relation to Phenylketonuria.*

Prof. J. N. Cumings (London): *Wilson's Disease.*

Dr. Paul Fourman (Cardiff): *Abnormal Calcium Metabolism.*

Prof. A. C. Frazer (Birmingham): *Diet and the Malabsorption Syndrome.*

This programme has been arranged as a contribution to the scientific aims of the 3rd International Congress of Dietetics to be held in London from 10 to 14 July 1961.

D. F. Hollingsworth,
(*Honorary Programmes Secretary*).

Ministry of Agriculture, Fisheries and Food,
Great Westminster House,
Horseferry Road,
London, S.W.1

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ELEANOR ROOSEVELT INTERNATIONAL CANCER FELLOWSHIP

The International Union Against Cancer, through funds made available by the Eleanor Roosevelt Cancer Foundation, will award annually fellowships for research on cancer. These fellowships have been created in the belief that the international exchange of scientists between centres with kindred interests will facilitate the sharing of knowledge and thereby contribute to the control of cancer.

These are senior postdoctoral awards designed for the support of persons who, as full-time members of the staff of universities, teaching hospitals, research laboratories or other institutions, have demonstrated interest and outstanding ability or promise as independant investigators in the field of research on basic cancer, its experimental and clinical aspects, and who wish to broaden their experience by a period of study in another country. The duration of the fellowships ordinarily will be one year but this period may be extended or shortened in special circumstances. The stipend will be based on the current salary of the applicant and the salary of persons of comparable qualifications in the place where the applicant expects to study. An allowance will be made for dependants and for costs of travel to and from the fellow's residence and the institution where he will work.

Application forms and additional information may be obtained from:

The International Union Against Cancer, P.O. Box 400, Geneva 2, Switzerland.

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INTERIM SOUTH AFRICAN COUNCIL OF THE COLLEGE OF GENERAL PRACTITIONERS

The College Council in London have now advised that the terms of reference for the Interim South African Council are agreed to as follows:

1. To co-ordinate the activities of the faculties of the College in South Africa.

2. To supervise and stimulate the work of members and associates of the College in South Africa.

3. To represent the College Council in South Africa

4. To further the liaison between the College Council and the South African faculties.

5. To comment on applicants for membership of the College from South Africa.

6. To plan financial support for the South African Council of the College.

PREPARATIONS AND APPLIANCES

ENAVID

AN ORAL CONTRACEPTIVE WITH ADDITIONAL GYNAECOLOGICAL INDICATIONS

The revised dosages which have been evolved during extensive clinical trials lasting over 5 years have necessitated the introduction of an **Enavid** 5 mg. tablet.

The simplified dosages now mean that most gynaecological disorders are treated with **Enavid**, many of them with the same dosage schedule.

For example, menorrhagia, irregular menstruation, dysmenorrhoea, premenstrual tension, amenorrhoea, oligomenorrhoea are all controlled by one 5 mg. tablet, administered from day 5 for 20 days in each of 3 menstrual cycles. This same dosage prevents ovulation during the treated cycles.

Details of the new dosage for metrorrhagia, advancement or postponement of menstruation, endometriosis, threatened or habitual abortions and infertility due to inadequate luteal phase are available on request from:

Keatings Pharmaceuticals Ltd., P.O. Box 256, Johannesburg. (*Telephone*: 23-6591).

PREDSOL RETENTION ENEMA

FOR THE TREATMENT OF ULCERATIVE COLITIS

Description: **Predsol** Retention Enema consists of a disposable plastic bag containing 20 mg. of prednisolone as the water-soluble disodium phosphate in isotonic buffered solution. It is ready for immediate use and provides a convenient means of self-administration for the treatment of ulcerative colitis.

Indications:— Chronic Ulcerative Colitis. One of the most recent forms of chemotherapy has been the use of corticosteroids. Water-soluble prednisolone in the form of the stable disodium phosphate results in an improvement in sigmoidoscopic appearance of the colon which can be confirmed histologically.

Method of Use: In practice the use of **Predsol** Retention Enema is very simple and effective, and easily undertaken by the patient at home. The enema is used each night on retiring. When in bed and lying on the left side with knees drawn up, the patient removes the stopper from the bag, lubricates the nozzle with petroleum jelly and gently inserts about half the length of the nozzle into the rectum. The bag is then slowly rolled up like a tube of toothpaste, taking a minute or two to introduce the solution gradually. When completed, the nozzle is removed, at the same time ensuring that no solution flows back into the bag, which is discarded. The patient should then roll over to lie face down for 3-5 minutes and go to sleep in any comfortable position.

Normally one **Predsol** Retention Enema will be used nightly for about a month and improvement can be anticipated in the majority of patients. This will usually occur early in treatment. Should no response occur there seems little point in continuing and other possible methods of treatment should then be considered. Some patients may relapse after an interval but are likely to show a similar response to a repeated course of treatment. If infection is a significent factor, specific therapy should be given.

Full instructions for use are included in each pack.

Side Effects: Little risk is involved from local application, particularly when the amounts employed approximate those normally given systemically. Careful observation during clinical use has failed to reveal any systemic undesirable effects from rectal instillation of prednisolone.

Mode of Issue: **Predsol** Retention Enema is supplied in 100 ml. disposable plastic bags in boxes of seven.

Further information is obtainable from:

Glaxo-Allenburys (S.A.) (Pty.) Limited, P.O. Box 485 Germiston.

BOOK REVIEW

HUMAN ANATOMY

Anatomy of the Human Body. By R. D. Lockhart, M.D., Ch.M., F.R.S.E., G. F. Hamilton, B.Sc., M.B., Ch.B., and F. W. Fyfe, M.A., M.B., Ch.B. (1959. Pp. 677 + Index. With 965 Figs. R10.50 net).
London: Faber and Faber Ltd.

As a break-through on the teaching front in anatomy, this book represents an achievement of the first magnitude. By attention to brevity and conciseness in the text, thorough annotation of illustrations and careful marrying of text to drawings, the authors have been able to produce a reference volume equal to about half the size of standard texts.

Unconventional presentation of material is a feature of the book, which makes its perusal a delight to the reader. The motto of the authors has been 'a little picture is worth a million words.' They have implemented this policy brilliantly. This is particularly well exemplified in the section on the nervous system, where a series of figures has been produced 'showing the nerve tracts and nuclei in stereoscopic sequence in longitudinal extent accompanied in their course by adjacent cross-sections at important levels, so that the student may be adequately equipped for his subsequent physiological studies' (p. vii).

There is a plenitude of illustration in colour as well as in black and white. There are close on 1,000 figures distributed through text numbering only some 700 pages.

The emphasis at all stages, on clinical applications, makes the study of anatomy intelligible and interesting to the undergraduate student. It also makes the volume invaluable to the clinician, who will find that its pages constitute an excellent source of revision and reference.

The muscles and their attachments and the description and illustration of the joints are done so effectively that the volume should have a particular appeal to students of physical medicine.

The purpose of the authors has been 'to lighten the burden of the student of anatomy.' In this they have succeeded most admirably and with great distinction.